COMPUTATIONAL MODELLING OF MICRONEEDLE INSERTION AND THERAPEUTIC DRUG DELIVERY

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Introduction

Microneedles, (MN) can pierce through the tough stratum corneum (SC) layer and reach the dermis directly, resulting in enhanced therapeutic efficacy. However, due to an incomplete understanding of the micro-biomechanics of skin absorption and subsequent therapeutics, MN performance often disappoints in clinical translation. This study aims to couple a state-of-the-art skin tissue model which reflects in *vivo* skin mechanical conditions with a constitutive equation of drug diffusion in tissue.

Research Questions:

A. Can a computational model accurately capture MN penetration?
B. With a better MN penetration model, can we better predict drug diffusion in coated MNs?
C. Can we experimentally validate the model by inserting drug-coated MNs into skin?

Methodology

Skin tissue is a 3D hyperelastic, anisotropic, multi-layered, heterogeneous porous media model.

- For insertion modelling, the stiff, isotropic stratum corneum was modelled using the Neo-Hookean model, while the dermis was modelled with the Gasser-Ogden-Holzapfel (GOH) model. [1].

$$\bar{\Psi}(\bar{C}, H_i) = \bar{\Psi}_g(\bar{C}) + \sum_{i=1,2} \bar{\Psi}_{fi}\left(\bar{C}, H_i(a_{0i}, k)\right)$$

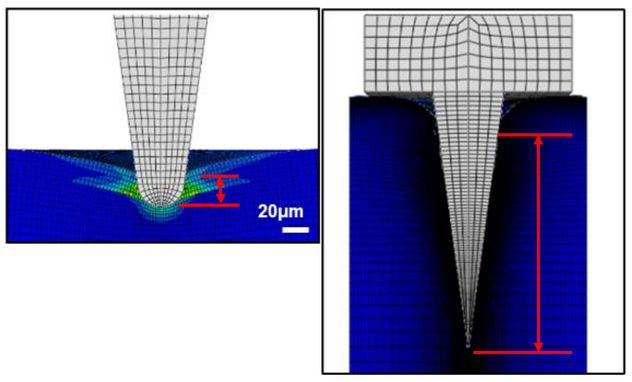
- For strain-dependent diffusion modelling, the aqueous pore pathway hypothesis defines an effective diffusion coefficient (***Deff***) dependent on a Hindrance factor (***H***), Tortuosity (***τ***) and Porosity (***ø***) as follows: [2].

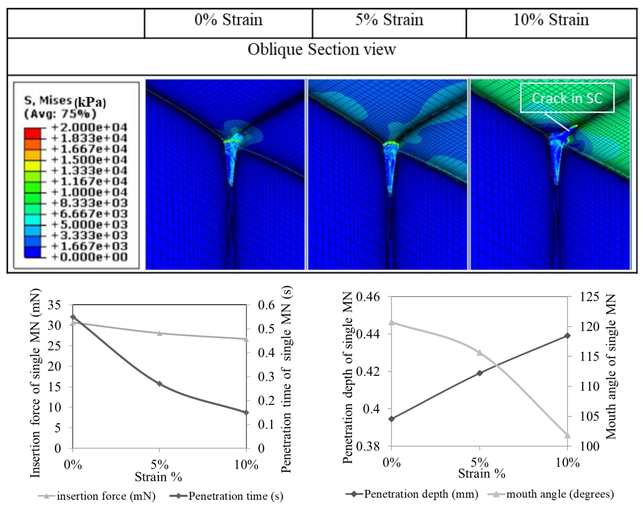
$$D_{eff} = \frac{\phi}{\tau} D^{\infty} H(\lambda)$$

Results

- Finite Element (FE) Models of MN penetration should consider the effects of in *vivo* skin tension and geometric effects of MN arrays [3]

Skin pretension affects both microneedle penetration force and penetration efficiency.





Penetration Force = Force at Penetration of SC

$$\text{Penetration Efficiency (\%)} = \frac{\text{Deformation Distance}}{\text{Length of Needle}}$$

Figure 2. Visualisation of MN penetration into the skin with varying levels of stretch at the travelled displacement of 0.5mm.

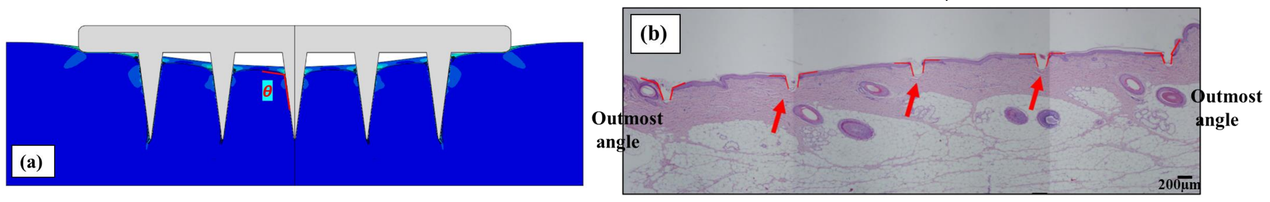


Figure 3. The visualisation of mouth angle results from FEA during penetration at travelled displacement of 2.4mm (a) and (b) A representative histology section of porcine skin [3].

Rigid, flat backing plates normal to the microneedles limit the penetration efficiency by up to 24%; Adjacent microneedles impact on the overall performance of the microneedle patch.

- FEA models of Transdermal drug delivery with Drug-coated Microneedle should consider the skin deformation and compression

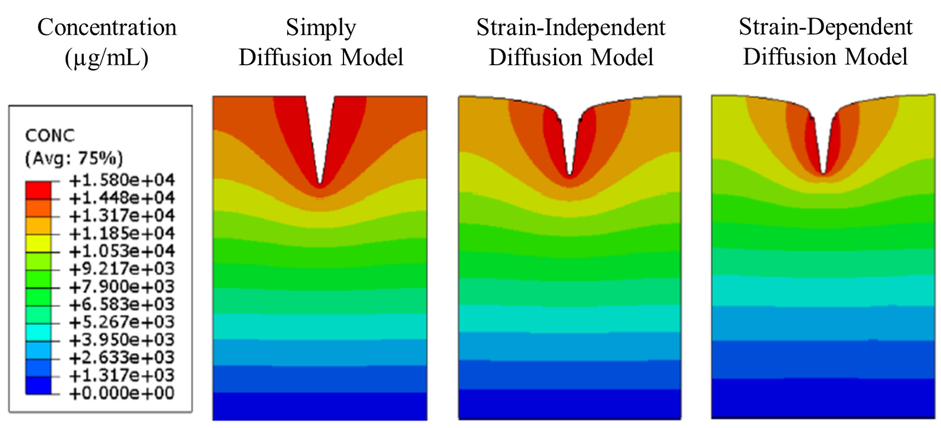


Figure 4. Concentration profiles for drug diffusion modelling.

There is a 40% difference in permeation efficiency when Fick diffusion models consider realistic needle insertion performance due to skin tension and deformation

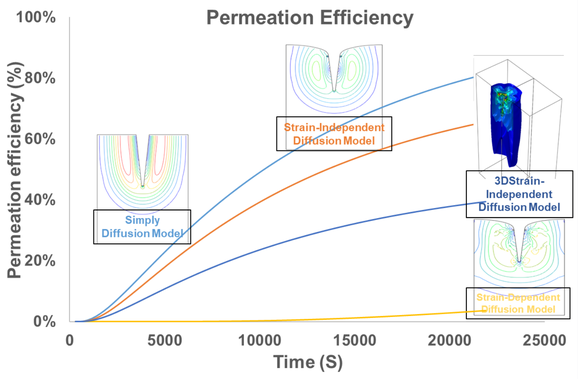


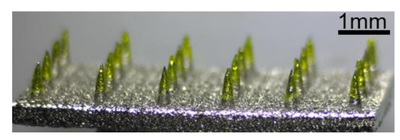
Figure 5. Comparison of Permeation efficiency at varying conditions.

Conclusion:

- Uniquely, our FEA model can reflect in vivo skin conditions accurately, and the effects of in vivo skin tension and geometric considerations of microneedle arrays
- This model can be a valuable tool in understanding drug distribution within the skin after microneedle insertion

On-going Work:

- Optimising and automating Drug Coating for 3D printed stainless steel Microneedle Patches



- The quantitative analysis of in vitro drug diffusion using Franz cell assay
- Experimental insertion of drug-coated MNs into skin to validate diffusion model

References:

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